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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,572	01/14/2004	Sharon Cohen-Vered	68518-A/JPW/GJG/JBC	5919

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EXAMINER	
DESAI, ANAND U	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 06/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/758,572	COHEN-VERED ET AL.	
	Examiner	Art Unit	
	Anand U. Desai, Ph.D.	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19,21,31,32,41-43,52,53 and 57-61* is/are pending in the application.

4a) Of the above claim(s) *19,21,32,41,43 and 52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18,31,42,53 and 57-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20041004,20041014*. ₱ 20050304
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-18, 31, 42, 53, 57, and 58, drawn to a pharmaceutical composition in the reply filed on September 27, 2004 is acknowledged. The traversal is on the ground(s) that an incorrect analysis has been used to support the requirement for restriction. Applicants contend no process of manufacturing the pharmaceutical composition is cited. Applicant is referred to Muller et al. U.S. Patent 6,407,079 B1, which discloses a method of producing pharmaceutical compositions comprising a sparingly water-soluble drug (see Abstract and claim 18). Further, Applicant contends that purported basis of the restriction between the method of use of Group II (claim 19), and the product of Group I is contrary to the explicit language of claim 19, and therefore fails to show that the method of claim 19 can be practiced with a materially different product. As stated in the restriction, the process for using the product as claimed can be practiced with another materially different product, such as steroids, and therefore the inventions can be shown to be distinct.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 19, 21, 32, 41, 43, and 52 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on September 27, 2004. This application contains claims 19, 21, 32, 41, 43, and 52 drawn to an invention nonelected with traverse in Paper filed September 27, 2004. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37

CFR 1.144) See MPEP § 821.01. New claims 59-61 have been added. Claims 1-18, 31, 42, 53, 57-61 are currently pending and under examination.

Priority

3. Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 119(e). The priority date is January 14, 2003.

Information Disclosure Statement

4. The information disclosure statements (IDSs) submitted on October 4, 2004, October 14, 2004, and March 4, 2005 are being considered by the examiner.

Claim Objections

5. Claims 1, 12, 16, and 59-61 are objected to because of the following informalities:

6. In claims 1, and 12, the last phrase describes a "composition", suggest the claim state, "...the pharmaceutical composition has a pH..." as recited in the preamble of the claims.

7. In claim 16, the last phrase describes a "composition", suggest the claim state, "...the pH of the pharmaceutical composition is between 7.5 and 8.5."

8. In claims 59-61, the last phrase describes a "composition", suggest the claim state, "...the water content of the pharmaceutical composition is less than .."

Appropriate correction is required.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 1-18, 31, 42, 53, and 57-61 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13, 24, 25, 37, 48, and 52 of copending Application No. 10/758,397 (U.S. Patent Application Publication 2005/0008634 A1). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in the copending application are drawn to a pharmaceutical composition comprising an aqueous carrier, a solubility enhancer including a substituted β-cyclodextrin, and a pharmaceutically acceptable salt of a peptide having the structural formula SEQ ID NO: 6, and disclosed in the current pending application as SEQ ID NO: 1. The claims of the copending application are also drawn to a lyophilized pharmaceutical composition, and a packaged pharmaceutical composition comprising a packaging material along with a predetermined amount of the lyophilized pharmaceutical composition.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 31, 42, and 53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. Claims 31, 42, and 53 are product claims that depend from withdrawn process claims. It is unclear what the pharmaceutical products are encompassing as currently claimed.

14. In claim 58, what is the predetermined amount?

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 1-4, 7, 8, 11, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mozes U.S. 2004/0127408 A1 (Priority date = February 26, 2001) in view of Hora et al. U.S. Patent 5,997,856.

Mozes discloses peptides and pharmaceutical compositions for the treatment of systemic lupus erythematosus. Mozes discloses a 19-mer peptide sequence identified as SEQ ID NO: 6, which has 100% identity with current application SEQ ID NO: 1 (see U.S. Publication '408, paragraphs 21, 67, and claims 2, and 9). Mozes does disclose the salt of the peptide, including

an acetate salt (see U.S. Publication '408, paragraphs 15, 88, and claim 1). Mozes discloses a pharmaceutical composition comprising the peptide and a pharmaceutically acceptable carrier (see U.S. Publication, '408, claims 24, and 25). Mozes does not explicitly disclose a pharmaceutical composition comprising a pharmaceutically acceptable salt of a peptide and a substituted β-cyclodextrin.

Hora et al. disclose the solubilization and/or stabilization of polypeptides, especially proteins, using cyclodextrin selected from the group consisting of hydroxypropyl, hydroxyethyl, glucosyl, maltosyl, and maltotriosyl derivatives of β-cyclodextrin (see entire document, particularly col. 11, line 59 through col. 12, line 17). Hora et al. disclose protein, hydroxypropyl β-cyclodextrin compositions that have proteins at concentrations ranging from 0.25 mg/ml to 1 mg/ml (see U.S. Patent '856, col. 22, Table 2). Hora et al. also describes a lyophilized composition comprising a polypeptide and a stabilizing/solubilizing amount of cyclodextrin selected from the group consisting of hydroxypropyl, hydroxyethyl, glucosyl, maltosyl and maltotriosyl derivatives of β-cyclodextrin (see U.S. Patent '856, col. 12, lines 10-15, and col. 22, Table 2, column describing type).

One would have been motivated to manufacture the pharmaceutical composition comprising an aqueous carrier, a pharmaceutical acceptable salt of the peptide disclosed by Mozes with the β-cyclodextrin derivatives disclosed by Hora et al., because of the enhanced solubilization and stabilization of the peptide in the β-cyclodextrin derivative solution. Therefore, it would have been obvious to the person having ordinary skill in the art to manufacture the pharmaceutical composition comprising an aqueous carrier, a pharmaceutical acceptable salt of the peptide identified as SEQ ID NO: 1 that is disclosed by Mozes, along with

the β-cyclodextrin derivatives disclosed by Hora et al. to treat systemic lupus erythematosus (current application, claims 1-4, 7, 8, 11, and 31). Furthermore, it would have been obvious to the person having ordinary skill in the art lyophilize the composition comprising the peptide disclosed by Mozes, and the β-cyclodextrin derivatives disclosed by Hora et al., because Hora et al. disclose a lyophilized polypeptide/ β-cyclodextrin composition (current application, claims 42, 53, 57, and 59-61).

17. Claims 5, and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mozes U.S. 2004/0127408 A1 (Priority date = February 26, 2001) in view of Hora et al. U.S. Patent 5,997,856 as applied to claim 1-4, 7, 8, 11, 31, 42, 53, 57, and 59-61 above, and further in view of Anderson, B.D. and Flora, K.P (Chapter 34, pages 739-754, The Practice of Medicinal Chemistry, edited by Camille Georges Wermuth, Academic Press 1996).

Mozes and Hora et al. do not explicitly disclose a pharmaceutical composition having a pH between 6.5 and 8.5. Anderson, B. et al. disclose the ideal pH for injectable formulations to be the pH of blood, 7.4, while pH above 9 causes tissue necrosis, and pH below 3 causes extreme pain and phlebitis (see page 747, 3rd paragraph).

One would have been motivated to manufacture a pharmaceutical composition within the range of pH being between 6.5 and 8.5 to be able to administer an injectable pharmaceutical composition. Therefore, it would have been obvious to the person having ordinary skill in the art to manufacture a pharmaceutical composition comprising an aqueous carrier, a pharmaceutical acceptable salt of the peptide identified as SEQ ID NO: 1 that is disclosed by Mozes, along with

the β-cyclodextrin derivatives disclosed by Hora et al. with a pH between 6.5 to 8.5 to treat systemic lupus erythematosus (current application, claims 1-8, 11, and 31).

18. Claims 9, 10, and 12-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mozes U.S. 2004/0127408 A1 (Priority date = February 26, 2001) in view of Hora et al. U.S. Patent 5,997,856 as applied to claim1-4, 7, 8, 11, and 31 above, and further in view of Stella et al. U.S. Patent 5,134,127.

Mozes and Hora et al. do not disclose a pharmaceutical composition comprising a sulfobutyl ether substituted β-cyclodextrin. Stella et al. disclose the use of sulfoalkyl ether cyclodextrin derivatives as solubilizing agents for water insoluble drugs for oral, intranasal, or parenteral administration (see U.S. Patent '127, Abstract). Stella et al. disclose the use of sulfobutyl ether substituted β-cyclodextrin complexed to digoxin, progesterone, testosterone, and phenytoin (see U.S. Patent '127, Figure 4, 5, 7, 9, Tables 2-5, col. 14, line 35 - col. 15, line 17, and claim 8).

Applicant is also referred to MPEP 2144.05 Obviousness of Ranges. Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims

only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); >see also *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.");< ** *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

One would have been motivated to manufacture the pharmaceutical composition comprising an aqueous carrier, a pharmaceutical acceptable salt of the peptide disclosed by Mozes with the sulfobutyl ether substituted β-cyclodextrin derivatives disclosed by Stella et al., because of the enhanced aqueous solubilization, reduced toxicity, and reduced membrane disruption of the sulfobutyl ether substituted β-cyclodextrin derivative solution (see U.S. Patent '127, col. 3, line 9-16). Therefore, it would have been obvious to the person having ordinary skill in the art to manufacture the pharmaceutical composition comprising an aqueous carrier, a pharmaceutical acceptable salt of the peptide identified as SEQ ID NO: 1 that is disclosed by Mozes, along with the β-cyclodextrin derivatives disclosed by Stella et al. to treat systemic lupus erythematosus (current application, claims 1-4, 7-18, and 31).

Conclusion

19. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U. Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 7:00 a.m. - 3:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (517) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

May 27, 2005

JON WEBER
SUPERVISORY PATENT EXAMINER